(a) a pre- region of artemin as set forth in SEQ ID NO:54 or SEQ ID NO:55;

(b) a pro- region of artemin as set forth in SEQ ID NO:56 or SEQ ID NO:57; or

(c) a pre-pro- region of artemin as set forth in SEQ ID NO:58 or SEQ ID NO:59.

REMARKS

Claims 12, 15-27 and 39-40 are presently pending in the instant application. Claims 12, 17, 23, 25 and 27 have been amended. No new matter has been added.

Although claims 12, 25, 27 and 39 had previously been allowed and claims 15-24, 26 and 40 had previously been objected to for informalities, and Applicants had amended the claims to address the informalities, the Examiner now rejects all of the claims for reasons stated in the Office Action, paper no 22, mailed on April 8, 2002.

Rejections under 35 U.S.C. § 112, first paragraph

Enablement

Claim 27 stands rejected under 35 U.S.C. § 112, first paragraph for an alleged failure to provide a description sufficient to enable a skilled artisan to practice the claimed invention. Specifically, the Examiner alleges that the specification "while being enabling for a nucleic acid encoding a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 54-59, does not reasonably provide enablement for a nucleic acid encoding variant having at least 88% amino acid sequence identity to SEQ ID NO: 54-59."

Applicants have removed the language "(d) a polypeptide that is at least 88% identical to (a), (b) or (c)." The amendment to claim 27 renders the examiner's rejections moot. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, first paragraph
Written Description

Claim 27 stand rejected under 35 U.S.C. § 112, first paragraph, for an alleged failure to provide a description "in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner alleges that claim 27 is a genus claim, and the term variant means a protein having one or more amino acid substitutions, deletions, insertions and/or additions made to SEQ ID NO: 54-59. The Examiner contends that "the specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 54-59." Further, "since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 54-59 alone is insufficient to describe the genus."

Applicants respectfully assert that claim 27 does not recite the term "variant". Further, claim 27 has been amended to delete the language "(d) a polypeptide that is at least 88% identical to (a), (b) or (c)." As written, claim 27 does not require any substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 54-59. Accordingly, claim 27 does not recite a genus. Claim 27 is fully supported and described throughout the specification, such as at p. 25, lines 25-32. Applicants respectfully assert that a skilled artisan would reasonably conclude that the Applicants were in possession of the claimed invention at the time of filing the application.

Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 12, 15-22, 25, 26, 39 and 40 stand rejected under 35 U.S.C. § 112, second paragraph, for an alleged failure to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that claims 12 and 25 are vague and indefinite in the recitation of "8 contiguous amino acids" because it is unclear which polypeptide the 8 contiguous amino acids refers to.

Claims 12 and 25 have been amended to recite "wherein said fragment has at least 8 contiguous amino acids...". The amendment clarifies that the "8 contiguous amino acids" refers to the fragment of artemin. In other words, the fragment must be at least 8 contiguous amino acids long.

Claims 12, 15 and 25 stand rejected as allegedly indefinite in the recitation of the term "biologically equivalent".

Applicants respectfully assert that a skilled artisan would readily understand the term "biologically equivalent" recited in claims 12, 15 and 25. Throughout the specification, Applicants describe that artemin functions to promote survival of neurons. (e.g. p. 14, lines 5-9 and p. 15, line 18-21). Therefore, any amino acid sequence or polypeptide sequence that is "biologically equivalent" to artemin has the biological function of artemin, which is to promote survival in neurons. Further, at p. 21, lines 2-5, the Applicants state "[b]y retaining the biological activity, it is meant that the modified polypeptide can bind to and activate GFRα1/RET and/or GFRα3/RET expressed by a cell, although not necessarily at the same level of potency as that of the mature human

artemin polypeptide identified herein." Accordingly, Applicants respectfully assert that the term "biologically equivalent" is clear and respectfully request reconsideration and withdrawal of the rejection.

Claims 12, 15 and 25 stand rejected as allegedly indefinite in the recitation of the term "naturally occurring". Specifically, the Examiner contends that "it is unclear whether....the claim...encompasses...polynucleotides amplified from human cDNA, or only sequences produced by digestion with restriction enzymes of DNA isolated from tissue..., or...all polynucleotide sequences that encode the polypeptide."

Applicants respectfully assert that a skilled artisan would readily understand the term "naturally occurring". Without further limitation or explanation, the term is readily used in the art to mean a substance as it is found or occurs in nature. Applicants submit herewith sample references which demonstrate the usage of the term "naturally occurring" in the art. Likewise, Applicants use the term "naturally occurring" in the instant application to refer to the artemin polypeptide as it is found or occurs in nature.

The Examiner further contends that "it is unclear whether....the claim...encompasses...polynucleotides amplified from human cDNA, or only sequences produced by digestion with restriction enzymes of DNA isolated from tissue..., or...all polynucleotide sequences that encode the polypeptide." Applicants respectfully assert that the term "naturally occurring" does not refer to the polynucleotide of artemin. The term refers to the artemin polypeptide. Further, the polynucleotide encoding this naturally-occurring artemin may be produced by a number of methods. The claims, as written, are not intended to be product-by-process claims. Applicants, therefore, should not be limited to artemin polynucleotides produced by any particular process. Accordingly, Applicants respectfully assert that the term "naturally occurring" is clear and respectfully request reconsideration and withdrawal of the rejection.

Claim 12 stands rejected as allegedly indefinite for recitation of "active domain". The Examiner contends that "it is not clear what activity is required of the claimed domain."

The specification at p. 31, lines 25-30, discusses the term "active domain". Specifically, the specification describes: "these pan-growth factors are believed to be potent and multispecific growth factors that are useful in the treatment of a wide spectrum of degenerative diseases and conditions including conditions that can be treated by any or all of the parent factors from which the active domains were obtained." The "active domain" in claim 12, therefore, refers to that part of the TGFβ family members that is responsible for their growth factor functions, i.e. to promote survival in cells. As the claims recite, this activity of the active domain can be used to treat degenerate diseases. Accordingly, Applicants respectfully assert that the term "active domain" is not vague and indefinite and respectfully request reconsideration and withdrawal of the rejection.

Claim 23 stand rejected as allegedly indefinite as to "whether the polypeptide comprising a human or mouse artemin is one of the list comprising SEQ ID NO: 26, 29, 32, 40, 41 or if it is to be additionally encoded by the amino acid, e.g. as a fusion protein." Claim 24 is rejected insofar as it depends on claim 23.

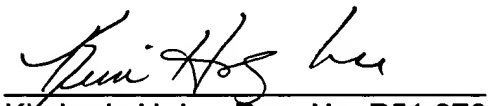
Claim 23 is not intended to recite a fusion protein. Claim 23 has been amended to clarify that the nucleic acid molecule encodes a polypeptide selected from the sequences identified by the listed SEQ ID NOs.

Applicants submit that all of the claims are clear and definite and respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

CONCLUSION

In summary, Applicants believe that they have overcome or obviated all of the Examiner's rejections and objections. Applicants submit that the application is in proper condition for allowance and respectfully request that such allowance be granted.

Respectfully submitted,



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MARKED-UP VERSION OF AMENDED CLAIMS

12. (Five times amended) An isolated polynucleotide encoding a pan-growth factor which polynucleotide comprises a nucleotide sequence encoding a naturally occurring artemin amino acid sequence or a fragment thereof that is biologically equivalent to artemin [and], wherein said fragment has at least 8 contiguous amino acids, wherein said nucleotide sequence comprises not more than 10,000 nucleotides, and wherein said artemin amino acid sequence is at least 88% identical to SEQ ID NO:26, and wherein said amino acid sequence promotes survival of neurons, and wherein said polynucleotide also comprises a nucleotide sequence encoding a polypeptide containing an active domain of at least one other growth factor from the TGF-β superfamily.

17. (Twice smended) The isolated and purified nucleic acid molecule of claim 15 comprising a nucleotide sequence encoding an artemin polypeptide [as set forth in] comprising SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:34, SEQ ID NO:35 or SEQ ID NO:36.

23. (Thrice amended) An isolated and purified nucleic acid molecule comprising no more than 10,000 nucleotides, wherein said nucleic acid molecule encodes a polypeptide selected from the group consisting of SEQ ID NOS: 3, 4, 5, 26, 29, 32, 33, 34, 35, 40, and 41, [and a polypeptide comprising a human or mouse mature artemin amino acid sequence,] wherein said artemin amino acid sequence promotes survival of neurons.

25. (Four times amended) An isolated nucleic acid molecule comprising an artemin nucleotide sequence, wherein the artemin nucleotide sequence encodes a naturally occurring artemin amino acid sequence selected from the group consisting of a pre-pro-artemin polypeptide, a pro-artemin polypeptide, a mature artemin polypeptide and a fragment of said pre-pro-artemin amino acid sequence that is biologically

equivalent to artemin [and] , wherein said fragment has at least 8 contiguous amino acids, and wherein the artemin amino acid sequence is at least 88% identical to SEQ ID NO:26 and wherein said amino acid sequence promotes survival of neurons.

27. (Four times amended) An isolated nucleic acid molecule comprising a polynucleotide encoding:

(a) a pre- region of artemin as set forth in SEQ ID NO:54 or SEQ ID NO:55;

(b) a pro- region of artemin as set forth in SEQ ID NO:56 or SEQ ID NO:57; or

(c) a pre-pro- region of artemin as set forth in SEQ ID NO:58 or SEQ ID NO:59[; or (d) a polypeptide that is at least 88% identical to (a), (b) or (c)].